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| **ATHEROSCLEROSIS** | | | |
| **Atherosclerosis**  **--Dz of the INTIMA** | * Initiated by Endothelial cells * INFLAMMATION IS THE FOUNDATION OF ATHEROSCLEROSIS * Endothelial injury 🡪 adhesions of monocytes and platelets 🡪 migration of monocytes and SMC into the intima🡪 SMC proliferate in the intima w/ ECM production 🡪 well developed plaque * Endothelial injury 🡪 ↑ in adhesion molecule (VCAM-1) 🡪 ↑ leukocyte adhesion (monocytes , and migration of monocytes into intima) * Accumulation of lipoproteins (LDL) in vessel wall * Monocyte adhesions to the endothelium 🡪 migration to the intima 🡪 transformation into macrophages and foam cells🡪 produce growth factors that leads to SMC proliferation and produce toxic oxygen species leading to oxidation of LDL in the lesions   + Hypercholesterolemia🡪↑ production of oxygen free radials🡪 lipid induced free radicals in macrophages or endothelial cells lead to oxidized LDL🡪 ingested by macrophages through scavenger receptors forms foam cells * Macrophages also recruit Lymphocytes (CD4 and CD8) to intima🡪 chronic inflammation (T cells stimulate macrophages, endothelium and SMCs) * Activated leukocytes + intrinsic arterial cells release fibrogenic mediators (cause fibrosis)🡪 proliferation of SMC🡪 production and deposition of dense ECM🡪 convert the fatty steaks into mature fibrofatty atheromas (initiated by PDGF releaced from platelets adherent to endothelial cells) 🡪advanced atheroma w/ fibrous cap 🡪 disruption of ribrous CAP w/ superimposed thrombus 🡪 can cause serious clinincal evens | Risk factors   * ↑ LDL ↓ HDL ↑ Lipoprotein a * Hypercholesterolemia (   + major lipids in plaques are cholesterol (cholesterol crystals) —oxidized LDL observed in macrophages in fatty streaks   + Genetic defects of lipid metabolism associated w/ accelerated atherosclerosis   + Other genetic acquired disorders (DM) lead to atherosclerosis   + ↓ level of serum cholesterol slows the progression of atherosclerosis   Morphology—can see dystrophic calcification  Complications   * rupture, ulceration, thrombosis, hemorrhage, aneurysm formation   Can cause abdominal (usually below renal arteries and above aortic bifurcation)aneurysms b/c …   * ↑ metalloproteinases (weakens healing and wall) * ↑ destruction of vessel walls * ↑ ischemia of vessel wall * ↑ common in men, elderly and smokers |
| **Monckeberg’s Arteriosclerosis** | * involves muscular arteries * usually in the lower limbs * patients usually >50 y/o and asx * see hard dilated vessels * Microscopically will see calcification s within the MEDIA |  |
| **HTN** | **Benign**—hyalinization; BP 150-160/88-90 and have HAD IT FOR YEARS  **Hyperplastic Arteriolosclerosis (Malignant HTN)**—rapid ↑ in BP; concentric laminated thickening of vessel walls (onion skinning); hyperplasia of SMC and thickened basement membrane; fibrinoid deposites and necrosis in vessels; usually diastolic is ↑ 110 | |

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|  | | **Defect** | **Lab Findings** |
| **Primary/Familial Hyperlipidemias** | | | |
| Type I (familial fat-induced hypertriglyceridemia) | | ↓ lipoprotein lipase (hydrolyzes triglycerides like the ones found in chylomicrons) | ↑ Triglycerides  **↑ chylomicrons**  normal VLDL  Normal or slightly ↑ cholesterol |
| Type IIa (hyperbetalipoproteinemia) | | LDL receptor deficiency | ↑ ↑ cholesterol  **↑ LDL** |
| Type IIb (combined hyperlipidemia) | | ↓ LDL receptors and ↑ APO B | ↑ ↑ cholesterol  ↑ LDL  **↑ VLDL**  Triglycerides slightly ↑ |
| Type III (carb-induced hypertriglyceridemia w/ hypercholesterolemia) aka dysbetalipoproteinemia | | Defect in APO E2 synthesis | ↑ cholesterol  ↑ VLDL  ↑ ↑ triglycerides  **↑ IDL** |
| Type IV (carb-induced hypertriglyceridemia w/o hypercholesterolemia) | | ↓ triglycerides elimination  ↑ triglyceride production | ↑ triglycerides  **↑ VLDL**  normal or slightly elevated cholesterol |
| Type V (combined fat and carb-induced hypertriglyceridemia) | | ↑ triglycerides production | ↑ ↑ ↑ triglycerides  **↑ VLDL and chlyomicrons**  normal or slightly elevated chylomicrons |
| **Acquired Hyperlipidemias** | Diabetes, Hypothyroidism, Nephrotic syndrome | | |

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| True  aneurysm | * Intact attenuated arterial wall or just dilations * Thinned ventricular wall * ***Saccular***—involving a seg. Of the vessel wall—only one side dilated * ***Fusiform***—diffuse circumferential dilation of a long vascular segment up to 20cm | * Artherosclerotic * Syphilitic * Medial cystic necrosis (Marfan sx) * Mycotic (infections) |
| False aneurysm | * Defect in the vascular wall leading to extravasc. Hematoma that freely communicated w/ the intravas. Space | * Ventricular rupture after an acute MI (cardiac tamponade) |
| Dissection | Tear in intima (not all the way through) —blood has entered the wall of the vessel | |

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| **Inflammatory Diseases of Blood Vessels** | | | | |  | | |
| **Condition** | **Etiology** | **Epidemiology** | **Location** | | **Lesions** | **Clinical** | **Labs** |
| **Aneurysms caused by… \*\*25% rupture risk for aneurysms >6 cm in diameter** | | | | | | | |
| **Atheriosclerotic** | Atherosclerosis | >50 y.o more in males | Abd aorta | **A** | | Could rupture expand and impinge on other structure |  |
| **Marfan Sx** | Disorder of CT  Defective synthesis of fibrillin-1 (essential for noaml eslatic development)🡪 aberrant TGF-β activity🡪weakinging of elastic tissue |  |  | Cystic medial necrosis in wall of the aorta –elastic fibers (usually in parallel arrays) now disrupted by pools of blue mucinous ground substance | | Manifestations in skeleton, eyes and CV system  Tall slender ppl, long extremities and fingers, Extopia lentis (sublaxation of lends), Prolapsed mitral valve, aortic regurg, aortic dilatation and dissection |  |
| **Loeys Dietz Sx** | Mutation in TGF-β receptors🡪 abnormalities in elastin and collagen I and II |  |  |  | |  |  |
| **Ehlers-Danlos Sx** | Defective type III collagen synthesis |  |  |  | |  |  |
| **Syphilis** | inflammation of the vaso vasorum inside vessel wall🡪ischemia of media🡪scaring (loss of elasticity)🡪dilatation🡪**TREE BARK APPEARANCE!!** | >40 y/o  stems from aortitis | Always in thoracic aorta (ascending) |  | | Could rupture expand and impinge on other structure |  |
| **Congenital Defects** | Berry aneurysms in cerebral arteries | 50 y/o and more freq in femailes |  |  | | Rupture🡪 subarachnoid hemorrhage |  |
| **Mycotic aneursms** | Infections (embolic or extensions) | Any age | Arterial Circulation |  | | Rupture |  |
| **Wegener Granulomatosis** | Necrotizing granulomatosis vasculitits  Hypersensitivity  Has lung involvement (multiple bilateral pulmonary nodules---NOT DIFFUSE!!!!) | >50 with male dominance | **1. Respiratory Tract**  **2. Kidneys** | **Necrotizing granulomas in respiratory system and glomerulitis** | | Clinical Triad   1. Sinusitis 2. Pneumonitis 3. Glomerulitis | **cANCA** |
| **Churg Straus** |  |  |  |  | | Asthma, skin rash, **eosinophilia, neuropathy** | **pANCA** |
| **Mircoscopic Polyangitis** |  |  | Lungs & Kidneys (like Wegener) but no skin |  | |  | **pANCA** |
| **Polyarteritis Nodosum (PAN)** | Transmural **necrotizing** **inflammation of med. Sized vessels** (not granulomatous) renal aa., not pulmonary aa. (chronic hypersensitivity)  NO LUNG INVOLVEMENT!!!! | **Young adults** with male predominance | Small and medium-sized arteries, e.g., kidneys, heart, liver and GI | Segmental, full thickness, fibrinoid necrosis w/ inflammation | | **Hepatitis B infection, hematuria, eosinophilia**  Renal hypertension (60%)  GI pain/bleeding (44%) | **pANCA** (RARELY)  eosinophilia  Bun/Cr ↑ b/c of renal probs |
| **Kawasaki Syndrome** | Mucocutaneous L.N. syndrome  Transmural inflammation w/ fibrinoid necrosis and **giant cells**  immune reaction to antigens🡪 activation of T cells and macros, B cell activation🡪 production of autoAb’s to endothelial cells🡪 **Vasculitis** | **Young children** (4-7 y/o) and infants; *most frequent cause of acquired heart disease in children in U.S.* | **Coronary arteries: MI**  **Temporal arteries: Blindness** | Resembles PAN; fibrinoid necrosis, marked transmural inflammation; aneurysms in coronary arteries | | Self limiting; **\*\*Treat: IVIg**  **Rash** (start on legs)  **High persistent fever (no response to meds for >5 days)**, cervical lymphadenitis  Cervical lymphadenitis  Cheilosis at corners of mouth  **Glossitis**: red beefy tongue  Conjunctival redness  \*Coronary angitis🡪can kill kid by causing aneurysms to the coronary artery🡪 actue MI  \*blindness is aneurysm in temporal artery | **Giant cells** |
| **Takayasu Arteritis** | **Granulomatous**  **inflammation** of aortic arch and its branches (why you get sx in arms and not the legs)  --Autoimmune |  | **Aortic arch and its branches** |  | | Weak pulse, coldness, low BP in arms |  |
| **Temporal Arteritis (Giant Cell)** | Immunologic reaction against vessel wall components, ex. elastic  Granulomatous inflamm of small and med. Sized artieres (usually branches of ext. carotid—mainly temporal a) | **>50 average age 75;** female predominance | Medium and small arteries principally cranial with **temporal involved 50-75%** | **Granulomatous inflammation of media w/ fragmentation of the internal elastic lamina and giant cells** | | Throbbing pain around temporal artery. **\*\*Treat w/steroids**  **Polymyalgia rheumatica**  **\*\*Blindness** | **Biopsy of 3+cm,  ESR ↑↑** |
| **Thromboangitis Obliterans (Buerger’s Disease)** | **\*\*Cigarette smoke**  **Direct toxicity of tobacco products to endothelial cells**  Endothelial hypersensitivity to tobacco products | Exclusively in smokers, young men and women Men>women | Segmental **thrombosing** acute and chronic inflammation of **arteries ,veins, and nerves** ***(pain)*** | Transmural inflammation with thrombosis containing **microabscesses** | | Early cold sensitivity followed by severe pain in affected part (usually in the legs); ulcerations of toes and maybe Frauk gangrene  Tx: quit smoking | Nothing specific |
| **Raynaud Disease** | **Paroxysmal pallor and cyanosis of fibers**  **Vasomotor response** to emotion and cold → vasospasm | **Young women *w/no underlying systemic dz*** | **Small arteries** and aterioles |  | | Pallor and cyanosis in extremities, nose, and tips of ears |  |
| **Raynaud Phenomenon** | **Arterial insufficiency** due to underlying systemic disease: SLE, Scleroder | Depends on **underlying disease** |  | |  |
| **Infectious Vasculitis** | * **Bacteria** * **Aspergillus** * **Mucor in diabetes (vascular damage esp in the eye)** |  |  |  | |  |  |
| **Varicose Veins** | * **Dilated tortuous veins** | Predisposing factors—obesity, heredity, age, posture (standing all day long) | Leg veins (pain, edema, stasis dermatitis), hemorrhoids (pain, bleeding)  Varicocele (in scrotum)  Esophageal varices (mean underlying liver problems!!, bleeding (portal HTN in cirrhosis) |  | |  |  |
| **Thrombophlebitis** | * **Thrombosis w/ or w/o inflammation** | Pregnancy (b/c compression of leg veins), obesity, tumors (cause migratory thrombophlebitis), prolonged bed rest, Heart failure (b/c not draining blood from vv. Properly) | Leg veins |  | | Can cause PE!!! | tumors (cause migratory thrombophlebitis)—  **in veins that are uncommon—like arms🡪 Trousseau sign** |

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| **Ischemic Heart Diseases & Myocarditis** | | | | | |
| **Disease** | Types/Clinical Picture | Risk Factors | Clues for Dx/Complications | Labs | |
| **Ischemic Heart Disease in General** | * Acute plaque change   + rupture/fissuring exposing the highly thrombogenic plaque constituents triggered by stress, abrupt changes in BP, adrenergic stimulation (MI incidence highest between 6 am and noon), ↑ platelets reactivity   + Erosion/ulceration exposing the thrombogenic subendothelial basement membrane to blood   + Hemorrhage into the atheroma expanding its volume * Inflammation (VERY IMPORTANT IN THE PATHOGENESIS OF ATHEROSCLEROSIS)   + Use highsensitivity CRP to predict the risk of coronary artery diseases * Thrombosis (in a partially occluded artery🡪 complete occlusion)—mural thrombi can embolize and clog distal vessels * Vasoconstriction   + Caused by circulating adrenergic agonists, locally released platelet contents, impaired secretion of endothelial cell relaxing factors * Effect—potential plaque disruption bc squeezing the plug   Reperfusion of myocardium within 20 MINUTES from onset of ischemia will PREVENT NECROSIS  Reperfusion injury--↑ permeability causing hemorrhage and edema🡪 endothelial damage   * Stunned myocardium🡪 reversible cardiac damage🡪 contractile dysfunction for up to 2 weeks post revascularization * Hibernating myocardium🡪 ischmia but viable myocardium🡪 exhibits contractile dysfunction🡪 more common in chronic ischemia setting🡪 can be reverseb by revascularization   + ↓ metabolism on PET FDG but not on PET w/ NH3 | | * **Key events in Myocytes**: Onset of ATP depletion🡪loss f contractility🡪 more ATP reduction🡪 irreversible cell injury w/in 40 min🡪 over an hr will have microvascular injury   **Key events in MI**   * 0-6h no change * 6-12: - gross mottling--microscopic hemorrhage * 12 few neutrophils * 12-24 gross yellowish center, hemorrhagic periphery * micro neutorphils (lots) * 24-4d same as above * 5-7d macrophages phagocytosis * 7-10d beginning granulation tissue (soft granulation tissue) * 10-14 good strong granulation * >14d healing beginning fibrosis * 5-7d, 7-10d important; myocardium soft dead tissue and stuff cleaning it up, so at risk of rupture, cardiac tamonade (esp 5-7d, lesser risk at 7-10d) | | |
| **Acute MI** | * Death of heart muscle   \*\*may have silent MI (no pain) in DM b/c of neuropathies to nerves of the heart!  ***Transmural MI***-- frequently there is plaque disruption occlusive plaque assoc. thrombus. 10% have no thrombus and are caused by vasospasm, emboli or other dz of coronary arteries.   * Necrosis the full thickness of ventricular wall🡪 perfused by single coronary artery-> cornonary atherosclerosis🡪 plaque disruption🡪 thrombus🡪 complete occlusion   ***Subendocardial MI***—VARIABLE!  Necrosis to 1/3rd 🡪 ½ of the ventricular wall🡪 perfused by more than one coronary artery🡪 shock, HTN or transient thrombus | Risk factors—HTN, DM, Hyperlipidemia, Obesity, Smoking, lipoprotein a, homocytseinemia, etc. | Crushing chest pain that commonly radiates to left shoulder   * Cardiogenic shock🡪 sudden death * Contractile dysfunction🡪 heart failure * Arrhythmias * Rupture🡪 cardiac tamponase (PULSUS PARADOXICUS) * Pericarditis * Mural thrombus * Ventricular aneurysm (true) * Rupture of papillary mm. (funational mitral regurg) | | CK   * CKMB ↑ w/in 2 hours and peaks at 12 hrs and back to normal w/in 3 days * CK index = CKMB/total CK \*100   Troponin i   * Specific to heart * 0.04🡪0.14 normal * >0.5 = MI!! * starts to elevate at 4-6 hrs and remains elevated for 6-9 days!! Useful for dx   Myoglobin   * ↑ 2-4 hours after infarct * peaks w/in 9-12 hours and goes back to normal w/in 1-2 days (first to return to normal) * tells type of MI (transmural ↑ more than subendo) and the size (↑ w/ size) |
| **Angina pectoris** | * Pain but no necrosis to heart muscle * ***Stable***🡪75% stenosis (chronic coronary stenosis) w/ no plaque disruption and no plaque assoc thrombus. Usually occurs w/ exercise * ***Unstable****🡪*frequently there is plaque disruption and usually non-occlusive plaque assoc. thrombus and often w/ thromboemboli. Occurs at rest and when you exercise * ***Prinzmetal*-**caused by coronary artery spasm—pain at rest |  |  | |  |
| **Chronic Ischemic heart dz w/ heart failure** | * Aka Ischemic cardiomyopathy—condition of elderly who develop progressive heart failure as a result of ischemic myocardial damage | * Post infarction * Severe atherosclerosis w/o infarction but have myocardial dysfunction |  | |  |
| **Sudden cardiac death** | * Usually SEVERE stenosis w/ frequent plaque disruption and often small platelet aggregates or thrombo and/or thromboemoboli. |  | * Acute myocardial ischemia w/ arrhythmias * Congential anomalies * Aortic stenosis * Mitral prolapse * Myocardidits * Myopathies * HTN heart * Cocaine (severe vasoconstriction & severe HTN) | |  |
| **Electrical abnormalities** | * Long QT syndrome * Congenital sick sinus sx—natural pacemaker is dysfunctional * Wolff-parkinson-white sx—patient has extra electrical activity of the hears🡪 episodes of tachycardia and sudden death * Many caused by mutation of genes encoding ion channels (Na, K, Ca( |  |  | |  |
| **Myocarditis** | * Inflammation of the myocardium * Direct—primary infection of the heart * Indirect/secondary: infection somewhere else (like strep)🡪 cross rxt of Abs to the heart * Major causes—viruses (esp coxsackievirus; borrelia/lyme dz can cause heart block) * Clinical picture—asx, fever, malaise, pericardial pain, sudden onset of acute heart failure * Drug induce: chemotherapeutic agents |  |  | | Necrosis of myocytes  Lymphocyte infiltrate b/c most are viral causes! (wont see this in MI)  Hypersensitivity (eosinophils)  Giant cell  Chagas (will see trypanosomes & eosinophils) |
| **Other Myocardial Dz** | * Drug induce: chemotherapeutic agents * Amyloidosis (usually in multiple myeloma pts) * Iron overload (hemosiderin w/in myocytes) * Hyperthyroidism🡪 hypertrophy of the heart * Hypothyroidism🡪 swelling of myofibers, interstitial edema🡪Myxedema heart |  |  | |  |

LAD supplies apex anterior surface of LV and anterior 2/3 of ventricular septum

Left circumflex supplies posterior aspect of the septum